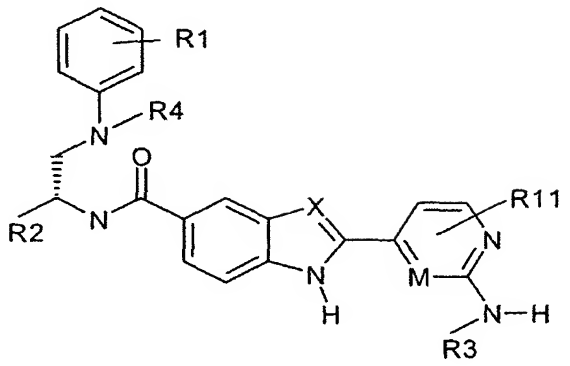
Patent Claims:

We Claim:

1. A compound of the formula I,



(I)

wherein:

X is N or CH;

M is N or CH;

R1 is hydrogen,
halogen chosen from F, Cl, I and Br,
-(C_1-C_4)-alkyl,
-CN,
-CF_3,
-OR^5, wherein R^5 is hydrogen or -(C_1-C_4)-alkyl,
-$N(R^5)$-R^6, wherein R^5 and R^6 are selected from hydrogen and -(C_1-C_4)-alkyl,
-$C(O)$-R^5, wherein R^5 is hydrogen or -(C_1-C_4)-alkyl, or
-$S(O)_x$-R^5, wherein x is the integer zero, 1 or 2, and wherein R^5 is hydrogen or -(C_1-C_4)-alkyl;

R2 is a heteroaryl radical, which is selected from 3-hydroxypyrro-2,4-dione, imidazole, imidazolidine, imidazoline, indazole, isothiazole, isothiazolidine, isoxazole, 2-isoxazolidine, isoxazolidine, isoxazolone, morpholine, oxazole, 1,3,4-oxadiazole, oxadiazolidinedione, oxadiazolone, 1,2,3,5-oxathiadiazole-2-oxide, 5-oxo-4,5-dihydro[1,3,4]oxadiazole, 5-oxo-1,2,4-thiadiazole, piperazine, pyrazine, pyrazole, pyrazoline, pyrazolidine, pyridazine, pyrimidine, tetrazole, thiadiazole, thiazole, thiomorpholine, triazole and triazolone, wherein the

heteroaryl radical is optionally substituted one, two, or three times by -C(O)-R^5, wherein R^5 is selected from hydrogen and –(C_1-C_4)-alkyl, –(C_1-C_4)-alkyl, -O-R^5, wherein R^5 is selected from hydrogen and –(C_1-C_4)-alkyl, -N(R^5)-R^6, wherein R^5 and R^6 are each selected from hydrogen and –(C_1-C_4-alkyl), halogen, or a keto radical,

-C(O)-OR^5, wherein R^5 is hydrogen or –(C_1-C_4-alkyl), or

-C(O)-N(R^7)-R^8, wherein R^7 and R^8 are each selected from hydrogen, -(C_1-C_4)-alkyl-OH, -O-(C_1-C_4)-alkyl and –(C_1-C_4-alkyl);

R3 is hydrogen or –(C_1-C_4-alkyl);

R4 is a heteroaryl radical, which is selected from pyrrole, furan, thiophene, imidazole, pyrazole, oxazole, isoxazole, thiazole, isothiazole, tetrazole, 1,2,3,5-oxathiadiazole-2-oxides, triazolones, oxadiazolone, isoxazolone, oxadiazolidinedione, triazole, 3-hydroxypyrro-2,4-diones, 5-oxo-1,2,4-thiadiazoles, pyridine, pyrazine, pyrimidine, indole, isoindole, indazole, phthalazine, quinoline, isoquinoline, quinoxaline, quinazoline, cinnoline, β-carboline and benzofused cyclopenta derivatives or cyclohexa derivatives of the heteroaryl radical, wherein the heteroaryl radical is optionally substituted one, two or three times by -(C_1-C_5)-alkyl, -(C_1-C_5)-alkoxy, halogen, nitro, amino, trifluoromethyl, hydroxyl, hydroxy-(C_1-C_4)-alkyl, methylenedioxy, ethylenedioxy, formyl, acetyl, cyano, hydroxycarbonyl, aminocarbonyl or -(C_1-C_4)-alkoxycarbonyl, or

an aryl radical which is selected from phenyl, naphthyl, 1-naphthyl, 2-naphthyl, biphenylyl, 2-biphenylyl, 3-biphenylyl and 4-biphenylyl, anthryl and fluorenyl, wherein the aryl radical is optionally substituted one, two, or three times by –(C_1-C_5)-alkyl, -(C_1-C_5)-alkoxy, halogen, nitro, amino, trifluoromethyl, hydroxyl, hydroxy-(C_1-C_4)-alkyl, methylenedioxy, ethylenedioxy, formyl, acetyl, cyano, hydroxycarbonyl, aminocarbonyl or -(C_1-C_4)-alkoxycarbonyl; and

R11 is hydrogen,
halogen chosen from F, Cl, I and Br,
-(C_1-C_4)-alkyl,
-CN,
-CF_3,
-OR^5, wherein R^5 is hydrogen or -(C_1-C_4)-alkyl,
-N(R^5)-R^6, wherein R^5 and R^6 are selected from hydrogen and -(C_1-C_4)-alkyl,
-C(O)-R^5, wherein R^5 is hydrogen or -(C_1-C_4)-alkyl, or
-S(O)$_x$-R^5, wherein x is the integer zero, 1 or 2, and wherein R^5 is hydrogen or -(C_1-C_4)-alkyl,

or a stereoisomer or a mixture of stereoisomers in any ratio of the compound, or a pharmaceutically acceptable salt of the compound, stereoisomer or mixture of stereoisomers of the compound.

2. The compound according to claim 1, wherein

X is N or CH;

M is N or CH;

R1 is hydrogen,
halogen chosen from F, Cl, I and Br,
-(C_1-C_4)-alkyl,
-CN,
-CF_3,
-OR^5, wherein R^5 is hydrogen or -(C_1-C_4)-alkyl,
-$N(R^5)$-R^6, wherein R^5 and R^6 are selected from hydrogen and -(C_1-C_4)-alkyl,
-C(O)-R^5, wherein R^5 is hydrogen or -(C_1-C_4)-alkyl, or
-$S(O)_x$-R^5, wherein x is the integer zero, 1 or 2, and wherein R^5 is hydrogen or -(C_1-C_4)-alkyl;

R2 is a heteroaryl radical, which is selected from imidazole, isothiazole, isoxazole, 2-isoxazolidine, isoxazolidine, isoxazolone, 1,3,4-oxadiazole, oxadiazolidinedione, 1,2,3,5-oxadiazolone, oxazole, 5-oxo-4,5-dihydro[1,3,4]oxadiazole, tetrazole, thiadiazole, thiazole, triazole and triazolone, wherein the heteroaryl radical is optionally substituted one, two, or three times by a keto radical, F, Cl, I, Br, or -(C_1-C_2)-alkyl, or
-C(O)-$N(R^7)$-R^8, wherein R^7 and R^8 are each selected from hydrogen, -(C_1-C_4)-alkyl-OH, -O-(C_1-C_4)-alkyl and –(C_1-C_4-alkyl);

R3 is hydrogen, methyl or ethyl;

R4 is a heteroaryl radical which is selected from the group of unsaturated, partially saturated or completely saturated rings which are derived from pyridine, pyrazine, pyrimidine, pyridazine, pyrrole, furan, thiophene, imidazole, pyrazole, oxazole, isoxazole, thiazole, triazole and isothiazole, wherein the heteroaryl radical is optionally substituted one, two or three times by -(C_1-C_4)-alkyl, –(C_1-C_4)-alkoxy, F, Cl, I, Br, nitro, amino, trifluoromethyl, hydroxyl, hydroxy-(C_1-C_4)-alkyl, methylenedioxy, ethylenedioxy, formyl, acetyl, cyano, hydroxycarbonyl, aminocarbonyl or

–(C_1-C_4)-alkoxycarbonyl, or

phenyl, wherein the phenyl is optionally substituted one, two or three times by F, Cl, I, Br, CF_3, -OH, -(C_1-C_4)-alkyl or -(C_1-C_4)-alkoxy; and

R11 is hydrogen,
halogen chosen from F, Cl, I and Br,
-(C_1-C_4)-alkyl,
-CN,
-CF_3,
-OR^5, wherein R^5 is hydrogen or -(C_1-C_4)-alkyl,
-$N(R^5)$-R^6, wherein R^5 and R^6 are selected from hydrogen and -(C_1-C_4)-alkyl,
-$C(O)$-R^5, wherein R^5 is hydrogen or -(C_1-C_4)-alkyl, or
-$S(O)_x$-R^5, wherein x is the integer zero, 1 or 2, and wherein R^5 hydrogen or -(C_1-C_4)-alkyl.

3. The compound according to claim 1, wherein the compound is:

N-[(S)-2-diphenylamino-1-(5-oxo-4,5-dihydro[1,3,4]oxadizol-2-yl)ethyl]-2-(2-methylaminopyrimidin-4-yl)-1H-indole-5-carboxamide,

N-{1-carbamoyl-2-[(4-fluorophenyl)pyridin-2-ylamino]ethyl}-2-(2-methylaminopyrimidin-4-yl)-1H-indole-5-carboxamide,

N-[(S)-1-(5-oxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)-2-(phenylpyridin-2-ylamino)ethyl]-2-(2-methylaminopyrimidin-4-yl)-1H-indole-5-carboxamide,

N-{1-carbamoyl-2-[(4-fluorophenyl)pyridin-2-ylamino]ethyl}-2-(2-aminopyrimidin-4-yl)-1H-indole-5-carboxamide,
N-[2-[(4-fluorophenyl)pyridin-2-ylamino]-1-(4H-[1,2,4]triazol-3-yl)ethyl]-2-(2-methylaminopyrimidin-4-yl)-1H-indole-5-carboxamide,

N-[1-carbamoyl-2-(phenylthiazol-2-ylamino)ethyl]-(S)-2-(2-methylaminopyrimidin-4-yl)-1H-indole-5-carboxamide,

N-[1-methoxycarbamoyl-2-(phenylpyridin-2-ylamino)ethyl]-(S)-2-(2-methylaminopyrimidin-4-yl)-1H-indole-5-carboxamide,

N-{1-carbamoyl-2-[(phenyl)pyridin-2-ylamino]ethyl}-2-(2-aminopyrimidin-4-yl)-1H-indole-5-carboxamide,

N-{1-carbamoyl-2-[(phenyl)pyrimidin-2-ylamino]ethyl}-2-(2-methylaminopyrimidin-4-yl)-1H-indole-5-carboxamide,

N-[1-(2-hydroxyethylcarbamoyl)-2-(phenylpyrimidin-2-ylamino)ethyl]-2-(2-methylaminopyrimidin-4-yl)-1H-indole-5-carboxamide,

(S)-2-{[2-(2-methylaminopyrimidin-4-yl)-1H-indole-5-carbonyl]amino}-3-[phenyl-(4-trifluoromethylpyrimidin-2-yl)amino]propionic acid,

N-{1-carbamoyl-2-[(4-fluorophenyl)-(5-methylpyrimidin-2-yl)amino]ethyl}-2-(2-methylaminopyrimidin-4-yl)-1H-indole-5-carboxamide,

N-((S)-1-carbamoyl-2-diphenylaminoethyl)-2-(2-methylaminopyrimidin-4-yl)-1H-benzimidazole-5-carboxamide,

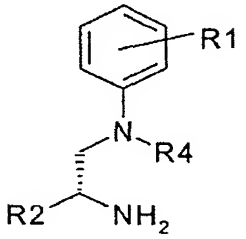
N-{1-carbamoyl-2-[(phenyl)pyrimidin-2-ylamino]ethyl}-2-(2-methylaminopyrimidin-4-yl)-1H-benzimidazole-5-carboxamide, or

N-{1-carbamoyl-2-[(phenyl)pyridin-2-ylamino]ethyl}-2-(2-methylaminopyrimidin-4-yl)-1H-benzimidazole-5-carboxamide,

or a stereoisomer or a mixture of stereoisomers in any ration of the compound, or a pharmaceutically acceptable salt of the compound, stereoisomer or mixture of stereoisomers of the compound.

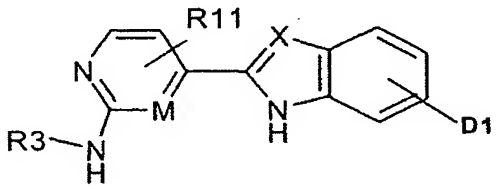
4. A process for preparing a compound according to claim 1, comprising,

a) reacting a compound of formula IV,



(IV)

wherein R1, R2 and R4 are as defined above,
with an acid chloride or an activated ester of the compound of the formula III,



(III)

wherein D1 is –COOH and R11, X, M and R3 are as defined above, in the presence of a base, or where appropriate, in the presence of a dehydrating agent in solution, and converting the product into a compound of the formula I,

b) separating the compound of the formula I, which has been prepared by method a) and which, on account of its chemical structure, appears in enantiomeric forms, into the pure enantiomers by means of forming salts with enantiomerically pure acids or bases, chromatography on chiral stationary phases or derivatization using chiral enantiomerically pure compounds such as amino acids, separating the resulting diastereomers and eliminating the chiral auxiliary groups, and

c) isolating the compound of the formula I which has been prepared by methods a) or b) in free form, or

d) converting it into physiologically tolerated salts when acidic or basic groups are present.

5. A pharmaceutical composition comprising a pharmaceutically effective amount of the compound according to claim 1 and a pharmaceutically acceptable carrier.

6. A method for producing a pharmaceutical for the prophylaxis and therapy of a disease associated with an increased activity of IκB kinase, in a patient in need thereof, comprising administering to such patient a pharmaceutically effective amount of a compound according to claim 1.

7. The method according to claim 6, wherein the disease is a chronic disease of the locomotory apparatus, a degenerative joint disease, diabetes Type II, inflammatory bowel disease, loss of cartilage following joint trauma or a relatively long period of joint immobilization following meniscus or patella injuries or ligament ruptures, a disease of the connective tissue, a disease which is due to overexpression of tumor necrosis factor alpha (TNFα) or an increased concentration of TNFα, atherosclerosis, stenoses, ulceration, Alzheimer's diseases, muscle breakdown, cancer, cardiac infarction, gout, sepsis, septic shock, endotoxic shock, viral infections, a disease caused by adenoviruses or herpesviruses, parasitic infections, a chronic inflammatory lung disease, acute synovitis, tuberculosis, psoriasis, diabetes, treatment of an acute or chronic rejection reaction on the part of the organ recipient against the transplanted organ, a chronic graft-versus-host disease, or an inflammatory vascular diseases.

8. The method according to claim 7 wherein the chronic disease of the locomotory apparatus is inflammatory, immunologically or metabolism-mediated acute or chronic arthritis, arthropathy, or rheumatoid arthritis.

9. The method according to claim 7 wherein the degenerative joint disease is osteoarthrosis or spondylosis.

10. The method according to claim 7 wherein the disease of the connective tissue is collagenosis, a periodontal disease, myalgia or a disturbance of bone metabolism.

11. The method according to claim 7 wherein the disease due to overexpression of tumor necrosis factor alpha (TNFα) or an increased concentration of TNFα is cachexia, multiple sclerosis, craniocerebral trauma, Crohn's disease or intestinal ulcers.

12. The method according to claim 7 wherein the viral infection is flu, hepatitis, HIV infection or AIDS.

13. The method according to claim 7 wherein the parasitic infection is malaria, leprosy, a fungal infection, a yeast infection, or meningitis.

14. The method according to claim 7 wherein the chronic inflammatory lung disease is chronic bronchitis or asthma.